PATENT COOPERATION TREATY

M.H

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 14 January 2000 (14.01.00)	
International application No. PCT/CA99/00437	**Applicant's or agent's file reference** 13045-2PCT
International filing date (day/month/year) 13 May 1999 (13.05.99)	**Priority date** (day/month/year) 08 June 1998 (08.06.98)
Applicant SULLIVAN, Robert et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

06 December 1999 (06.12.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Olivia RANAIVOJAONA
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
13045-2PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00437	13/05/1999	08/06/1998
International Patent Classification (IPC) or national classification and IPC A61K39/00		
Applicant IMMUCON INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06/12/1999	21.07.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer BROCHADO GARGANTA, M Telephone No. +49 89 2399 8935

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00437

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-8,10-21	as originally filed			
9	as received on	24/06/2000	with letter of	15/06/2000

Claims, No.:

1-4	as received on	24/06/2000	with letter of	15/06/2000

Drawings, sheets:

1/9-9/9	as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☒ the claims, Nos.: 5-8
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1 and 2.

because:

☒ the said international application, or the said claims Nos. 1 and 2, with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4
	No:	Claims	
Inventive step (IS)	Yes:	Claims	4
	No:	Claims	1-3
Industrial applicability (IA)	Yes:	Claims	3, 4
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item I

Basis of the report

1. The amendments filed on 24.06.00 do not introduce additional subject-matter, which extends beyond the content of the application as filed. Therefore, the amendments meet the requirements of Article 34(2) PCT.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1 and 2 are directed to the use of a compound for immunocontraception of a male or female.

   The Applicant should be aware that such a subject-matter is considered by this Authority, as a matter belonging to the private and personal sphere of a human being, and therefore not susceptible of industrial application (see Guidelines IV-4). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   (A) Bérubé B. et al.: Biology of Reproduction, vol. 51, 1994, pages 1255-1263

   (B) Boué F. et al.: Biology of Reproduction, vol. 51, no. 4, page 577-587

   (C) WO 97 40 386 A

2. Novelty

2.1 The subject-matter of claims 1 and 2, referring to the use of an antigenic fragment of a P34 protein for immunocontraception of a male or female object, is new in the sense of article 33(2) PCT, because this use is not disclosed in the prior art.

2.2 Claim 3 discloses a immunocontraceptive vaccine for a male or female subject. Such a vaccine is not known from the prior art and therefore claim 3 is considered to be new (Article 33(2) PCT).

2.3 The probe as a marker for male or female fertility of claim 4 is new in the sense of Article 33(2) PCT, as this subject-matter is not disclosed in the prior art.

3. Inventive step

3.1 Document A, which is considered as being the closest state of the art, discloses the inhibition of *in vivo* fertilization by active immunization of male hamsters against a 26-kDa sperm protein, wherein a polyclonal antiserum is raised against P26H and the IgG fraction is added to an *in vitro* sperm-zona pellucida assay (see abstract). An involvement of the P26H in sperm-zona pellucida interaction is shown, as well as the **contraceptive effect of the active immunization of male hamsters with protein P26H**, due to an inhibition of gamete interaction (see pages 1259 and 1262).

Claim 1 is distinguished from document A by the **administration of a different antigenic fragment, that of P34 protein**, which elicits an immunocontraception response by said subject, said fragment showing a high specificity for said P34 protein.

The problem to be solved by the invention may therefore be regarded as to provide an alternative method for human immunocontraception, using a different antigenic fragment.

The skilled person would turn to document C, from which is known that **antibodies raised against P26H protein inhibit sperm-zona pellucida binding *in vitro*** (see page 577). Document C further discloses the inhibition of the human sperm-zona

pellucida interaction by an antiserum against a hamster sperm protein (see title), wherein the **search for an antigen on human spermatozoa homologous to the P26H** hamster spermatozoa protein is performed. Using polyclonal antibodies directed against said hamster protein, **an antigen with a molecular mass of 34 KDa could be identified**. This antiserum was used in processes leading fertilization, and does not affect the sperm motility, the acrosome reaction nor the zona-free hamster test. However, when added to a human sperm-zona pellucida assay, said serum interferes with sperm-zona binding (see page 578).

Therefore, it would be obvious for the skilled person in order to solve the posed problem to combine the features set out in documents B and C. Thus, claim 1 has not a basis on an inventive concept (Article 33(3) PCT).

3.2 For the same reasons, the additional features of claim 2 do not involve an inventive concept according to Article 33(3) PCT. After the identification and isolation of an antigen with a molecular mass of 34 kDa (see document C, page 578), it would be within the capabilities of a skilled person to further characterise this protein, starting obviously with the determination of the amino acid sequence and the correspondent encoding nucleic acid sequence, using standard techniques and without the need of an inventive concept.

3.3 The subject-matter of claim 3, referring to an immunocontraceptive vaccine, wherein the antigenic fragment of a p34 protein is administered together with a suitable pharmaceutically acceptable carrier, is also not based on an inventive concept as required by Article 33(3) PCT. It is common knowledge the fact that, for administering an antigenic fragment, a suitable carrier has to be present. For this reason and considering the reasoning given in 3.1, the skilled person would obviously arrive to the features of claim 3 without being inventive.

3.4 Document A discloses an antibody raised against P34 to be used for the diagnosis of male infertility, wherein the quantification of P34 is performed after hybridisation with formation of an immunocomplex (see claims 3 and 6, and pages 6-8).

The difference between this disclosure and the subject-matter of claim 4 is the fact that, this hybridisation is done at the nucleic acid level, using cDNA as a marker.

There is no indication in the prior art documents to use a cDNA sequence, capable of hybridising under stringent conditions with a human acrosomal sperm protein, as a marker. Thus, claim 4 is based on an inventive concept as required by Article 33(3) PCT.

4. For the assessment of the present claims 1 and 2 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States.

Cloning and sequencing of P26h cDNA

Poly(A)$^+$RNA from hamster and human testicular tissues was purified from total RNA solution using a poly(A)$^+$RNA purification kit (Pharmacia Biotech, Baie D'Urfé, QC) according to the supplier's instructions. The cDNA library was prepared according to the supplier's instructions. Briefly, testicular poly(A)$^+$RNA was reverse-transcribed and ligated into the lambda Uni-Zap^{TM} XR vector (Stratagene, La Jolla, CA). The lambda library was packaged and amplified using *Escherichia coli* XL1-Blue cells and screened with the random-prime labeled 710 bp P26h cDNA. The positive clones were isolated by plaque purification and the longest one (1081 bp) was subcloned into pBluescript KS+. All nucleotide sequences were determined by the dideoxinucleotide termination method (Sanger) using T7 Sequenase v 2.0 kit. The labeled reaction products were analyzed on a DNA sequencer gel. Sequence translation was performed using Gene Jockey software (Biosoft, Cambridge, UK).

***In situ* hybridization**

Tissue cryosections were fixed with freshly prepared 4% paraformaldehyde in PBS for 5 min. at RT (room temperature), incubated for 10 min. in 95% ethanol/5% acetic acid at -20°C and rehydrated by successive baths of decreasing concentrations of ethanol diluted with DEPC-H_2O. Target RNA was unmasked by enzymatic digestion with 10 µg/ml proteinase K (Boehringer Mannheim) in PBS for 10 min. at 37°C, followed by a 5 min. incubation in 0.2% glycine. Sections were postfixed for 5 min. with 4% paraformaldehyde in PBS, acetylated with 0.25% acetic anhydride, 0.1 M triethanolamine, pH 8.0, for 10 min. and finally washed with PBS.

Tissues were prehybridized for 1h with a preheated 250 µg/ml salmon sperm DNA in a hybridization

WHAT IS CLAIMED IS:

1. A method of immunocontraception of a male or female subject, which comprises administering to said male or female subject an antigenic fragment of a P34 protein to elicit an immunocontraception response by said male or female subject, said antigenic fragment of P34 showing a high specificity for said P34 protein.

2. A method according to claim 1, wherein said P34 protein is encoded by a sequence as set forth in SEQ ID NO:3, and wherein said antigenic fragment has an amino acid sequence selected from a group consisting of SEQ ID NO:4 and SEQ ID NO:5.

3. An immunocontraceptive vaccine for a male or female subject, which comprises an antigenic fragment of a P34 protein in association with a suitable pharmaceutically acceptable carrier, wherein said vaccine elicits an immunocontraception response by said male or female subject after its administration.

4. A probe as a marker for male or female fertility, which comprises a cDNA sequence capable of hybridizing under stringent conditions with a human acrosomal sperm protein P34.

5. A method for the diagnosis of male or female infertility, which comprises the steps of:

a) determining the amount of human P34 protein in a sperm or ovule sample; and

b) comparing the determined amount of step a) with a fertile control sample.

6. A method according to claim 5, wherein the amount of human P34 in step a) is determined using an antibody raised against the human P34 protein.

7. A kit for the diagnosis of male or female infertility, which comprises:

a) an anti-P34 antibody enzyme-labeled;

b) an enzyme substrate; and

c) a fertile control sample.

8. A kit according to claim 7, which comprises a calibration curve for the amount of human P34 obtained using the fertile control sample of step (c).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
13045-2PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 99/ 00437	13/05/1999	08/06/1998
Applicant		
IMMUCON INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[X] contained in the international application in written form.

[X] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows.

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 99/ 00437

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1 and 2 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

[redacted] rnational Application No
T/CA 99/00437

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K39/00 C12Q1/68 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 40386 A (IMMUCON INC) 30 October 1997 (1997-10-30) the whole document ---	5-8
Y	BOUE F ET AL: "HUMAN SPERM-ZONA PELLUCIDA INTERACTION IS INHIBITED BY AN ANTISERUM AGAINST A HAMSTER SPERM PROTEIN" BIOLOGY OF REPRODUCTION,US,ORLANDO, FL, vol. 51, no. 4, page 577-587 XP002038410 ISSN: 0006-3363 abstract --- -/--	1,3

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 November 1999	29/11/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fernandez y Branas,F

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
Y	BERUBE B. ET AL: "Inhibition of in vivo fertilization by active immunization of male hamsters against a 26-kDa sperm glycoprotein" BIOLOGY OF REPRODUCTION, vol. 51, 1994, pages 1255-1263, XP002122660 abstract	1,3
A	BOUE F ET AL: "SURFACE LOCALIZATION OF P34H, AN EPIDIDYMAL PROTEIN, DURING MATURATION, CAPACITATION, AND ACROSOME REACTION OF HUMAN SPERMATOZOA" BIOLOGY OF REPRODUCTION,US,ORLANDO, FL, vol. 54, no. 5, page 1009-1017 XP002038412 ISSN: 0006-3363 page 1011, "sperm protein extraction"	1-8
A	US 5 753 231 A (HERR JOHN C ET AL) 19 May 1998 (1998-05-19)	1-3
A	US 5 756 299 A (GOLI SURYA K ET AL) 26 May 1998 (1998-05-26)	

1

INTERNATIONAL SEARCH REPORT

[redacted]tion on patent family members

[redacted]national Application No
[redacted]CT/CA 99/00437

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9740386 A	30-10-1997	US 5723305 A	03-03-1998
		AU 2284997 A	12-11-1997
		CA 2251964 A	30-10-1997
		EP 0906575 A	07-04-1999
US 5753231 A	19-05-1998	US 5602005 A	11-02-1997
		US 5436157 A	25-07-1995
		US 5605803 A	25-02-1997
		AT 176156 T	15-02-1999
		AU 649609 B	02-06-1994
		AU 5186290 A	26-09-1990
		DE 69032922 D	11-03-1999
		DE 69032922 T	30-09-1999
		EP 0461177 A	18-12-1991
		ES 2130121 T	01-07-1999
		JP 4505008 T	03-09-1992
		WO 9009802 A	07-09-1995
US 5756299 A	26-05-1998	AU 5594098 A	03-07-1998
		WO 9826076 A	18-06-1998

WO 99/64064
PCT/CA99/00437

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:
COTE, France
Swabey Ogilvy Renault
Suite 1600
1981 McGill College Avenue
Montréal, Québec H3A 2Y3
CANADA

Date of mailing (day/month/year) 16 December 1999 (16.12.99)	
Applicant's or agent's file reference 13045-2PCT	**IMPORTANT NOTICE**
International application No. PCT/CA99/00437	**International filing date** (day/month/year) 13 May 1999 (13.05.99)
Priority date (day/month/year) 08 June 1998 (08.06.98)	
Applicant IMMUCON INC. et al	

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,CN,EP,IL,JP,KP,KR,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   16 December 1999 (16.12.99) under No. WO 99/64064

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
J. Zahra

Telephone No. (41-22) 338.83.38

Continuation of Form PCT/IB/308

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

Date of mailing (day/month/year)	IMPORTANT NOTICE
16 December 1999 (16.12.99)	
Applicant's or agent's file reference	**International application No.**
13045-2PCT	PCT/CA99/00437

The applicant is hereby notified that, at the time of establishment of this Notice, the time limit under Rule 46.1 for making amendments under Article 19 has not yet expired and the International Bureau had received neither such amendments nor a declaration that the applicant does not wish to make amendments.